UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,200	03/04/2002	Todd Laurence Underiner	7772	9262

27752 7590 07/26/2005

THE PROCTER & GAMBLE COMPANY
INTELLECTUAL PROPERTY DIVISION
WINTON HILL TECHNICAL CENTER - BOX 161
6110 CENTER HILL AVENUE
CINCINNATI, OH 45224

EXAMINER	
STITZEL, DAVID PAUL	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 07/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/070,200	UNDERINER ET AL.	
	Examiner	Art Unit	
	David P. Stitzel, Esq.	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 14-16* is/are rejected.

7)☒ Claim(s) *1-15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/[illegible]/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Official Action

Acknowledgment of Receipt

Receipt of the Applicant's Election, *with traverse*, of claims 1-16, which was filed on November 23, 2004 in response to the Official Action mailed on November 5, 2004, is acknowledged. However, the applicants have failed to provide an appropriate rebuttal as to why the applicants are of the opinion that the examiner's restriction requirement was improper. Applicants' unsubstantiated statement that "applicants' select Group I [claims 1-16] with traverse," without more, is a mere assertion and thus found unpersuasive. Therefore, since the applicants did not distinctly and specifically point out the alleged errors in the examiner's restriction requirement, the election has been treated as an election *without traverse* pursuant to MPEP § 818.03(a). As a result, the restriction requirement is deemed proper and therefore made FINAL.

Status of Claims

Pursuant to the aforementioned election, claims 1-16 are currently pending and therefore examined herein on the merits for patentability.

Claim Objections - 35 U.S.C. § 112, Fourth Paragraph, & 37 C.F.R. 1.75(c)

The following is a quotation of the fourth paragraph of 35 U.S.C. § 112, which forms the basis of the claim objections as set forth under this particular section of the Official Action:

> Subject to the following paragraph, a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers.

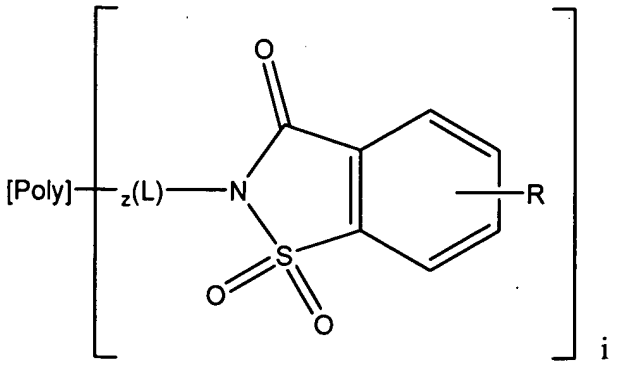
In addition, the following is an in-part quotation of the relevant portion of 37 C.F.R. 1.75(c), which also forms the basis of the claim objections as set forth under this particular section of the Official Action:

> One or more claims may be presented in dependent form, referring back to and further limiting another claim or claims in the same application. Claims in dependent form shall be construed to include all the limitations of the claim incorporated by reference into the dependent claim.

35 U.S.C. § 112, fourth paragraph, and 37 C.F.R. 1.75(c) both require that a claim in dependent form shall be construed to incorporate by reference all the limitations of the independent claim to which the dependent claim refers and that the dependent claim shall further limit the subject matter claimed in the independent claim. See MPEP 2164.08.

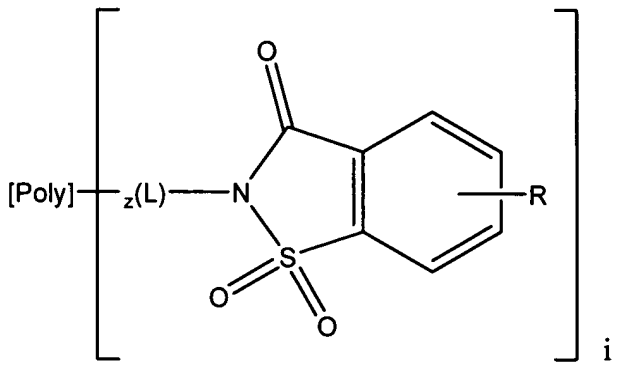
Claims 1-15 are objected to under both 35 U.S.C. § 112, fourth paragraph, and 37 C.F.R. 1.75(c) as being of improper dependent form for failing to further limit the subject matter of the independent claims to which the dependent claims refer. Therefore, applicants are required to cancel the dependent claims; amend the dependent claims so as to place the claims in proper dependent form; or rewrite the dependent claims in independent form.

More specifically, independent claims 1 and 14 are directed to a polymeric saccharin conjugate having a general formula comprising [Poly]-$(L)_z$-T, wherein [Poly] is a polymeric unit; $(L)_z$ is a linking group having a z value of 0 or 1; and T is a heterocyclic saccharin ring component capable of inhibiting enzymes. However, dependent claims 2-13 and 15 are directed to a polymeric saccharin conjugate having a general formula comprising:



wherein [Poly] is a polymeric unit; $(L)_z$ is a linking group having a z value of 0 or 1; T is a heterocyclic saccharin ring component capable of inhibiting target enzymes; and i has a value from 1 to 100.

If i has a value of 1, then dependent claims 2-13 and 15 further define and are within the scope of the subject matter claimed in independent claims 1 and 14, respectively. If on the other hand, i has a value from 2 to 100, dependent claims 2-13 and 15 are improperly dependant in that they fail to further limit, and are in fact no longer within the scope of, the subject matter claimed in independent claims 1 and 14, respectively. More particularly, independent claims 1 and 14, which are directed to a polymeric saccharin conjugate having a general formula comprising [Poly]-$(L)_z$-T, only have a single pendant heterocyclic saccharin ring component covalently bound to a polymeric unit through an optional linking group, whereas dependent claims 2-13 and 15, which are directed polymeric saccharin conjugates having a general formula comprising:



can alternatively have more than a single pendant heterocyclic saccharin ring component (i.e., when i has a value from 2 to 100) covalently bound to a polymeric unit through an optional linking group. In these particular instances, dependent claims 2-13 and 15 are improperly dependent in that they fail to further limit, and are no longer within the scope of, the subject matter claimed in independent claims 1 and 14, respectively, and thus fail to meet the statutory requirements as set forth by both 35 U.S.C. § 112, fourth paragraph, and 37 C.F.R. 1.75(c). ***It is therefore recommended that the applicants rectify the improper dependency by redrafting independent claims 1 and 14 to recite and include a polymeric saccharin conjugate having a general formula "[Poly]-$[(L)_z$-T$]_i$," wherein "i has a value from 1 to 100."***

Claim Rejections - 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112, which forms the basis of the claim rejections as set forth under this particular section of the Official Action:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-4, 6 and 15 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

More specifically, claim 2 is indefinite because the limitations as set forth in "a)" through "p)" of claim 2 fail to designate which variable is being further defined. If said limitations are further defining what may constitute the pendant R group of the aromatic ring for example, then the applicant should particularly point out that this is indeed the case by explicitly stating "wherein R is:" prior to "a)" in claim 2, thereby distinctly claiming that the following substituents or moieties are in fact further defining the pendant R group of the aromatic ring.

Furthermore, claims 2-4, 6 and 15, which contain the claim language "and mixtures thereof" following a plethora of various possible substituents, are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The specification is a mere recitation of the claim language and therefore fails to provide any guidance to one of ordinary skill in the art as to what particular substituents, and in what particular ratios, constitute a "mixture thereof." More importantly however is the fact that the claims are drawn to a single specific compound, namely a polymeric saccharin conjugate, and not to a composition comprising various components, which could constitute a "mixture thereof."

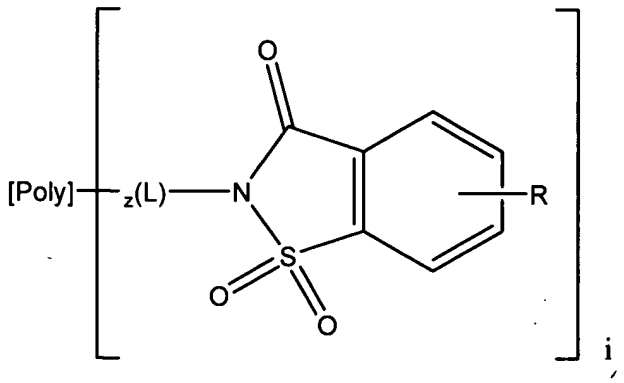
Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraph of 35 U.S.C. § 102, which forms the basis of the anticipation rejections as set forth under this particular section of the Official Action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-7 and 14-16 are rejected under 35 U.S.C. § 102(a) as being anticipated by the following scientific journal article, namely Koizumi, T., et al., "Radical Polymerization Behavior of N-Vinylsaccharin," Journal of Polymer Science: Part A: Polymer Chemistry, Vol. 37, 3419-3426 (1999) (hereinafter referred to as the "Koizumi" reference).

Independent claims 1, 14 and 16 of the instant application are directed to a polymeric saccharin conjugate having a general formula comprising [Poly]-$[(L)_z$-$T]_i$, wherein [Poly] is a polymeric unit; $(L)_z$ is a linking group having a z value of 0 or 1; and T is a heterocyclic saccharin ring component capable of inhibiting enzymes; and i has a value from 1 to 100. In addition, dependent claims 2-7 and 15 are directed to a polymeric saccharin conjugate having a general comprising:



wherein [Poly] is a polymeric unit; $(L)_z$ is a linking group having a z value of 0 or 1; T is a heterocyclic saccharin ring component capable of inhibiting target enzymes; and i has a value from 1 to 100. Similarly,

the Koizumi reference likewise discloses a polymeric saccharin conjugate having a general formula comprising [Poly]-$[(L)_z$-$T]_i$, wherein [Poly] is a polymeric unit; $(L)_z$ is a linking group having a z value of 0; and T is a heterocyclic saccharin ring component, which is inherently capable of inhibiting proteolytic enzymes; and i has a value greater than or equal to 1. See Koizumi at page 3420, Table II, top right structure, wherein: [Poly] is polyethylene; $(L)_z$ is a linking group having a z value of 0; and T is a heterocyclic saccharin ring component.

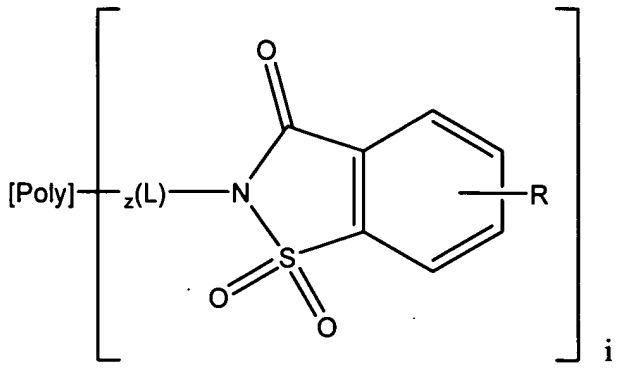
Claim Rejections - 35 U.S.C. § 103

The following is a quotation of the appropriate paragraph of 35 U.S.C. § 103, which forms the basis of the obviousness rejections as set forth under this particular section of the Official Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7 and 14-16 are rejected under 35 U.S.C. § 103(a) as being obvious in light of the combined teachings of: Buckingham, K.W., Berg, R.W., "Etiologic Factors in Diaper Dermatitis: The Role of Feces," Pediatric Dermatology, Vol. 3, No. 2, pp. 107-112, 107 (1986)(hereinafter the "Buckingham" reference); U.S. Patent Number 5,650,422, which issued to Dunlap et al. on July 22, 1997 (hereinafter the "Dunlap '422 patent"); and the Koizumi reference.

Independent claims 1, 14 and 16 of the instant application are directed to a polymeric saccharin conjugate having a general formula comprising [Poly]-$[(L)_z$-$T]_i$, wherein [Poly] is a polymeric unit; $(L)_z$ is a linking group having a z value of 0 or 1; and T is a heterocyclic saccharin ring component capable of inhibiting enzymes; and i has a value from 1 to 100. In addition, dependent claims 2-7 and 15 are directed to a polymeric saccharin conjugate having a general formula comprising:



wherein [Poly] is a polymeric unit; $(L)_z$ is a linking group having a z value of 0 or 1; T is a heterocyclic saccharin ring component capable of inhibiting target enzymes; and i has a value from 1 to 100. Claim 17 of the instant application is directed to a method for preventing human skin irritation comprising the step of contacting human skin with a composition comprising a polymeric saccharin conjugate having a general formula comprising $[Poly]-[(L)_z-T]_i$, wherein [Poly] is a polymeric unit; $(L)_z$ is a linking group having a z value of 0 or 1; and T is a heterocyclic saccharin ring component capable of inhibiting enzymes; and i has a value from 1 to 100.

A scientific journal article outlines a study that was conducted to define the role for feces in the etiology of diaper dermatitis by identifying specific irritants in the feces of diapered infants. Buckingham at page 107. This reference states in relevant part that feces are viewed as being important etiologically in diaper dermatitis. *Id.* This reference experimentally determined that the irritation potential of infant feces may be attributed largely to the presence of proteolytic and lipolytic enzymes and that these enzymes can irritate the skin directly. See Buckingham at page 111. However, Buckingham, fails to disclose any particular chemical compounds that may serve as efficacious inhibitors of proteolytic enzymes.

The Dunlap '422 patent disclosed that saccharin derivatives are efficacious proteolytic enzyme inhibitors (title and abstract). However, the Dunlap '422 patent does not disclose the covalent bonding of

saccharin derivatives, which are efficacious proteolytic enzyme inhibitors, as pendant groups to a polymeric backbone.

On the other hand, the Koizumi reference discloses a polymeric backbone having pendant saccharin molecules covalently bound thereto (title). However, Koizumi reference fails to mention the proteolytic enzyme inhibition characteristics of said pendant saccharin molecules.

It would have been obvious to one of ordinary skill in the art to covalently bind a saccharin derivative, which was known to possess efficacious proteolytic enzyme inhibition properties (as taught by the Dunlap '422 patent), to a polymeric backbone as pendant group (as taught by the Koizumi reference) to yield a polymeric saccharin therapeutic conjugate having efficacious proteolytic enzyme inhibition characteristics that would be useful for the treatment of diaper dermatitis, especially since it was illustrated by the Buckingham reference that diaper dermatitis is attributed to proteolytic enzymes directly irritating the skin. Sufficient motivation exists, as one of ordinary skill in the art would immediately envision the incorporation of a known proteolytic enzyme inhibitor, such as a saccharin derivative, onto a polymeric backbone and subsequent utilize said polymeric saccharin conjugate as an effective therapeutic for treating diaper dermatitis, which is caused by proteolytic enzymes irritating the skin. A reasonable expectation of success in combining the aforementioned references is present, as it was well known in the chemical and pharmaceutical arts as of the effective filing date of the instant application that active therapeutics can be covalently bound to polymeric backbones, such as polyethylene glycol (PEG) for example, to produce polymeric therapeutic conjugates having desired solubility characteristics while maintaining their therapeutically biologically active properties.

Remarks

The following is a list of scientific publications and prior art patents made of record and considered pertinent to the applicant's disclosure, but are not however currently relied upon in construing the claim rejections as set forth herein:

Pearce, G., et al., "Isolation and Characterization from Potato Tubers of Two Polypeptide Inhibitors of Serine Proteinases," *Archives of Biochemistry and Biophysics*, Vol. 213, No. 2, pp. 456-462 (February, 1982);

Berg, R.W., et al., "Etiologic Factors in Diaper Dermatitis: The Role of Urine," *Pediatric Dermatology*, Vol. 3, No. 2, pp. 102-106 (1986);

Otto, H.H., et al., "Cysteine Proteases and Their Inhibitors," Chemical Reviews, Vol. 97, No. 1, pp. 133-171 (1997);

Brocchini, S. and Duncan, R., "Pendent Drugs, Release from Polymers," The Encyclopedia of Controlled Drug Delivery, Wiley, N.Y., pp. 786-816 (1999);

U.S. Patent Number 4,496,689, entitled "Covalently Attached Complex of α-1-Proteinase Inhibitor with a Water Soluble Polymer," which issued to Mitra on January 29, 1985; and

U.S. Patent Number 5,681,811, entitled "Conjugation-Stabilized Therapeutic Agent Compositions, Delivery and Diagnostic Formulations Comprising Same, and Method of Making and Using the Same," which issued to Ekwuribe on October 28, 1997.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David P. Stitzel, Esq. whose telephone number is 571-272-8508. The examiner can normally be reached on Monday-Friday, from 8:30AM-6:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary L. Kunz can be reached at 571-272-0887. The central fax number for the USPTO is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published patent applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished patent applications is only available through Private PAIR. For more information about the PAIR system, please see http://pair-direct.uspto.gov. Should you have questions about acquiring access to the Private PAIR system, please contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DPS

GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600